

Rheumatology scheme

Definition: It is connective tissue disorder characterized by articular & extra-articular manifestations.

Aetiology:

- Most probably **autoimmune**
- **Genetic** factors may play a role (+ve family history & HLA association)
- **Environmental** factors play some role

Clinical picture:

A- Type of patient

- Female > male **except** in Gout, PAN & ankylosing spondylitis
- Rheumatoid arthritis: F:M = 3:1 - SLE: F:M = 9:1

- Type of patient
 - Articular (3Ds)
 - Others

- General
 - Extra-articular

B- General manifestations: F A H M

C- Articular manifestations: 3Ds

Distribution:

- 1- Number of the affected joints: mono or poly arthritis
e.g. RA & SLE ----- **poly** - acute **gout** ----- mono
- 2- Symmetrical or asymmetrical:-
All are asymmetrical **except** (RA & SLE both are symmetrical)
- 3- Small joints or large joints:- (RA & SLE both are small joints)
- 4- Peripheral or central: (RA & SLE: peripheral > central (**centripetal**))
- 5- Erosive or non erosive:
 - Non erosive: inflammation of synovial membrane only
 - Erosive: erode & destroy the cartilage as RA.

- Distribution
 - Description
 - Deformity

Description:

- | | |
|---------------------------|------------|
| 1- Redness | 2- Hotness |
| 3- Tenderness | 4- Swollen |
| 5- Limitation of movement | |

Deformity: in **erosive** only .e.g. Rh.A, chronic gout or psoriatic arthropathy.

D- Extra articular manifestations: 7

- | | |
|---------------------------|-----------------|
| 1. <u>C.V.S</u> | 2. <u>Chest</u> |
| 3. <u>Abdomen</u> | 4. <u>C.N.S</u> |
| 5. <u>Skin</u> | 6. <u>eye</u> |
| 7. <u>Blood & L.N</u> | |

Investigations:

- 1) X-ray: - Osteoporosis
 - Erosive diseases:- Narrow joint space ± Deformity (mention)
- 2) Aspiration of synovial fluid: Antibodies
- 3) Blood:-
 - a-CBC: - Anemia:- normocytic, microcytic or macrocytic
 - WBCs: increased **except** in SLE & Felty's syndrome
 - b) CRP: increased **except** in SLE (CRP may increases in SLE with infection)
 - c) ESR: elevated (marked elevation)

VISIT...

LANZAROTE
Caliente.COM

d) SGOT & SGPT: elevation may be drug induced or rarely liver affection.

4) Serological tests:

Non specific antibodies:- may be +ve in all reumatological diseases, inflammation or even in normal population.

Rheumatoid Factor (RF): +ve in **80%** of RA and 20% of SLE

Lupus Erythrematosis (LE) cells: +ve in **80%** of SLE and 20% of RA

Antinuclear antibody (ANA): +ve in **95-100%** of SLE and 30% of RA

Specific antibodies:

- 1- Anti CCP (cyclic citrullinated peptide) --- rheumatoid arthritis - **Specific**
- 2- Anti double stranded DNA: ---- **SLE (80%) - Specific**
- 3- Anti-sm (anti-smith Ab, NOT anti smooth muscle Ab): SLE - **Specific**
- 4- Anti Ro anti La: ---- SLE, Sjogren's syndrome
- 5- Anti histone antibody: drug induced SLE e.g. hydralazine
- 6- SCL 70 antibody: scleroderma
- 7- Anti-RNP (ribonucleoprotein):in mixed connective tissue disease

Differential diagnosis:

- DD of monoarthropathy (see later)
- DD of polyarthropathy (see later)

Treatment:

- Cortisone
- NSAIDs
- Immunosuppressive drugs: (methotrexate, cyclophosphamide)
- Physiotherapy

Rheumatoid arthritis

Def.: Chronic, symmetrical, poly-erosive synovitis of peripheral joints with extra-articular features

Incidence: 2 per 1000 population

Aetiology:

- Genetic predisposition: family history = HLA DR4
- Infection: viral (EBV) or atypical bacteria
- Autoimmune: (see theory of pathogenesis)

Theory

Initiating event unknown (may be **viral** infection) stimulates susceptible **T cells**.

The stimulated T released **lymphokines** which activate B and T cell proliferation (**IL1, IL6 & TNF**)

The B cells released **IgG** (usually disfigured)

The immune system released **IgM** (RF) against the formed IgG the antibody bonded together to form immune **complex**.

The formed immune complex fixed the complement and engulfed by PNL cells and lysozymes which initiate **synovitis**.

With **chronicity** the following changes were developed

- Angiogenesis
- Accumulation of inflammatory cells in the synovium
- Synovial cell proliferation (rapidly growing **pannus**)

Pathology (3 changes)

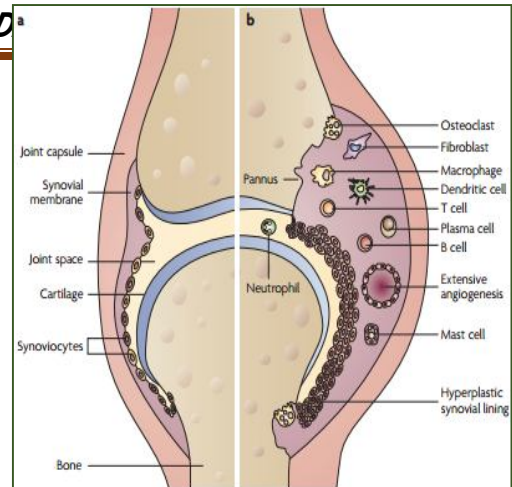
1- Arthritis:-

Hallmark of RA is hypertrophy of the synovial membrane

Firstly: **synovitis** with joint effusion

Then: outgrowth of granulation tissue (**pannus**) into and over the articular surface results in **destruction** of articular cartilage and subchondral bone

Lastly: **fibrosis** and **deformities**



2- Subcutaneous nodule (granuloma):-

Small-vessel vasculitis = area of central necrosis (fibrinoid) surrounded by macrophages and fibroblasts and a cuff of cellular connective tissue and chronic inflammatory cells.

3- Vasculitis: Usually involving small arteries.

- Type of patient - General
- Articular (3Ds) - Extra-articular
- Others (variants of RA)

Clinical picture:-

1- Type of patient:- F : M = 3:1 - Age of onset 20-40

2- General symptoms: may present firstly
Fever – malaise – loss of BW – anorexia

3- Articular (3Ds + complications)

Description:

- Morning **stiffness** for more than 1 hour (improved by movement)
- **Fusiform** swelling of the fingers (affection of PIP)
- Local sign of inflammation as swollen, red, warm with limitation
- **Soft tissue tender** swelling indicates thickened synovial



Distribution:

Polyarthritis:- Symmetrical polyarthritis of the **small peripheral joint**

The **wrist, MCP joints and PIP** joints are most commonly involved

The **DIP** are **usually spared** in rheumatoid arthritis

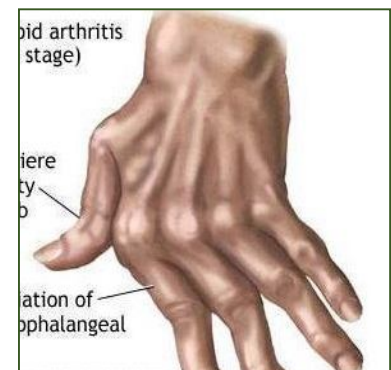
Later on proximal big joints may be affected (**centripetal**)

Special joint affected: tempromandibular – cricoarytenoid – sternoclavicular –
atlanto-axial are usually affected in RA

Mono/pauci- articular form rarely described in children

Deformity: Due to erosion and destruction of the joint surface, which impairs range of movement and deformity

- **Ulnar deviation:** fingers deviated toward the little finger.
- **Boutonniere deformity:** hyperflexion at PIP joint with hyperextension at DIP



- Swan neck deformity: hyperextension at PIP joint, hyperflexion at DIP.
- Z-Thumb deformity: fixed flexion and subluxation at the MP joint and hyperextension at the IP joint
- Hammer toes: subluxation of heads of MTP, shortening of extensor tendons
- Flexion contractures
- Triggered finger: caused by SC nodules

Complications:

1. Joint deformities (see above): **disability** and disuse atrophy (Ms **wasting**)
2. Atlanto-axial and subaxial subluxation: **spinal cord** compression
3. Tenosynovitis: may cause **rupture** of tendons
4. Compression of **carpal tunnel**: thenar atrophy, tingling of thumb, index finger, and middle finger
5. Ruptured **Baker's cyst** (outpouching of synovium behind the knee) DD from acute thrombophlebitis (DVT).

Function classification: Disability

- **Class I:** no restrictions
- **Class II:** moderate (**perform normal activities**)
- **Class III:** marked (**can't perform activities of usual occupation/self-care**)
- **Class IV:** incapacitation (**wheelchair**)

4- Extra-articular

1- C.V.S

- Pericarditis
- Myocarditis
- Endocarditis
- HTN
- IHDs
- AR occurs due to vasculitis (not endocarditis)

2- Chest

- Pleurisy
 - Pulmonary infarction
 - Caplan's syndrome:- rheumatoid nodules with pneumoconiosis (very rare)
- Interstitial pulmonary fibrosis
 - Pulmonary hypertension

3- Abdomen:

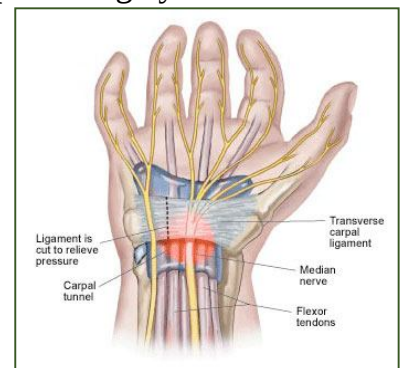
- Nausea & vomiting
- Abdominal pain due to vasculitis
- Pancreatitis
- Renal (Lupus nephritis)
- Esophagitis
- Gastritis & peptic ulcer
- Hepatosplenomegaly

4- C.N.S

- Psychosis
- Depression
- Neuropathy
- Cerebral vasculitis ----- stroke
- Chorea
- Epilepsy
- Myopathy
-

- **Carpal tunnel syndrome**: compression of the median nerve due to hypertrophied synovium, it may be the first symptom of R.A.

- **Atlanto-axial syndrome:-** spinal cord compression ----- paraplegia



5- Skin:

- **Subcutaneous nodule:**

Description:- Few millimeters to a few centimeters in diameter



Distribution:- (tendon sheath or extensor surfaces) Usually over bony prominences (olecranon, the calcaneal tuberosity, the metacarpophalangeal joints) or other areas that sustain repeated mechanical stress

Nodules associated with a positive RF titer and severe erosive arthritis

- **Palmer erythema**
- **Vasculitis**
- **Pallor**

6- eye: - Conjunctivitis

- Scleritis ----- repeated attack ----- scleromalacia (blue sclera)
- Iritis is not common

7- Blood & L.N: Aneamia:-

- Normocytic normochromic anemia (autoimmune hemolytic anemia)
- Microcytic hypochromic anemia (iron deficiency anemia)
- Macrocytic anemia (Methotrexate)

5- Others:-

Variant of Rheumatoid arthritis

1- Sjogran syndrome: (type 2) (sicca syndrome):

- Arthritis (like RA)
- Dry eye (**xerophthalmia**), dry mouth (**xerostomia**)
- Lymphadenopathy:- there is increased incidence of lymphoma
- **Renal tubular acidosis & Raynaud's phenomenon**
- +ve rheumatoid factor in **90%** of cases

2- Felty's syndrome:

- Arthritis (like RA)
- Hepatosplenomegaly with hypersplenism, lymphadenopathy
- Pancytopenia
- Cortisone is drug of choice

3- Seronegative arthropathies: (sero -ve spondylopathy) (See later)

General features: 8 features

- Rheumatoid factor: **negative** (the reason for the name)
- **Central** (spondylitis and / or sacroilitis) > peripheral arthritis (**centrifugal**)
- **Asymmetrical** peripheral arthritis
- **HLA-B27** (associated disorders)
- +ve family history
- **Eye:- Red**
- **Erythema**
- **Enthesitis** (inflammation at sites of tendon insertion)

4- Still disease: (systemic onset juvenile arthritis)

- A disease of under-fives but adult cases may occur
- Fever, skin rash, splenomegaly
- RF: -ve
- Late arthropathy. so, misdiagnosed as haematological disorder

Investigations: as scheme

1) X-ray:

- Osteoporosis
- Narrow joint space
- Deformity (mention)
- X-ray chest: pleural effusion



2) Aspiration of synovial fluid: Antibodies

3) Blood:

- RBCs: **anemia** (normochromic - hypochromic)
- WBCs: ↑↑ may ↓↓ in felty's syndrome
- ESR: ↑↑↑ may > 100 in severe cases
- CRP: ↑↑

4) Serological tests:

- 1- RF: +ve in about 80% of cases

Rheumatoid factor (RF):

- Mainly IgM directed against Fc of IgG
- Positive in about 85% of RA patients
- **Non specific** for RA but usually used for follow up & severity evaluation

Methods:

Latex (synthetic material - Rose-Welar (sheep RBCs) - Bentonite (clay)

False positive:

5% of healthy people	10-20% of people over age 65
Other sero-positive diseases	SBE
Bacterial and viral infections	Gammopathy – granuloma

- 2- LE: +ve in 20% of cases

- 3- ANA: +ve in 20% of cases

- 4- Recently: **anti CCP** (cyclic citrullinated peptide)

The most common tests for anti-citrullinated protein antibodies (ACPAs) are the anti-CCP (cyclic citrullinated peptide) test and the Anti-MCV (anti-mutated citrullinated Vimentin).

Recently a serological point-of-care test (POCT) for the early detection of RA has been developed. This assay combines the detection of rheumatoid factor and anti-MCV for diagnosis of RA and shows a sensitivity of 72% and specificity of 99.7%

Diagnostic Criteria (American Rheumatism Association, 1987)

(4 or more of the following)

1. Morning stiffness (> 1 hour) **for > 6 weeks**
2. Soft tissue swelling of 3 or more joint areas **for > 6 weeks**
3. Arthritis in at least 1 of : MCP, PIP or wrist **for > 6 weeks**
4. Symmetric arthritis **for > 6 weeks**
5. Rheumatoid nodules
6. Serum RF
7. X-ray changes: erosions or periarticular osteopenia

Treatment of RA:

A) General treatment

- *Rest*: especially during acute stage
- *Splinting*: ↓ pain, prevent deformity
- *Physiotherapy*: it can be started when the acute phase disappears

B) Medical treatment:

1- NSAIDs: for relive of pain & inflammation

- Aspirin 500 mg/4h
- Diclofenac 50 mg. t.d.s.
- Paracetamol 500 mg t.d.s.
- Indomethacin 50 mg t.d.s.
- Ketoprofen 100 mg t.d.s.

- 1- NSAIDs
- 2- Cortisone
- 3- Disease modifying (DMARDs)
- 4- Immuno suppressive

Mechanism: ↓ ↓ PG through inhibition of **cyclo-oxygenase** enzyme.

S/E: Nephrotoxicity, hepatotoxicity, peptic ulcer

2- Cortisone:

- Small dose of cortisone may be given (7.5 mg/d)
- May be used in high dose in treatment of extra-articular manifestations
- SE of cortisone: see endocrinology

Analgesic & cortisone improve pain only - no effect on joint damage or disease progression.

3- Disease modifying anti-rheumatic drugs (DMARDs):

- Reduced **activity** of the disease (↓ ESR, CRP) & ↓ progression
- These drugs are **slow** acting drugs (their effect take 4-8 weeks to appear)

Drug	Doses	Side effects and percussion
Sulfasalazine		GITD – rash – neurological disease – megaloblastic anaemia
Gold (Aurothiomalate)	50 mg/week IM for 20 weeks (total dose: 1000 mg)	- BM Depression (Stop if WBCs < 3000 or platelets < 100000) - Hypersensitivity - Proteinuria (Stop if proteinuria > 2g/24h)
Penicillamine	250 mg/d	As Gold + SLE
Chloroquine	250 mg/d	Corneal opacity, GIT irritation, skin rash fundus examination (regular)

4- Immuno suppressive:

i) Methotrexate:

- **DOSE:** 7.5 mg/week
- **S/E:** Hepatotoxicity – Nephrotoxic – Megaloblastic anemia

ii) Leflunomide: (Avara) anti pyrimidine:

- 100 mg/d for 3 days then 20 mg/d

Tumor necrosis factor α (TNF α) blockers:- in severe active rheumatoid arthritis when DMRDs therapy has failed. (usually given in combination with methotrexate)

- The onset of action is rapid compared with traditional DMRDs (2 weeks)
- e.g.: **Infliximab**, Adalimumab **S.E: T.B.**

Interleukin – 1 blocker (anakinra):- It blocks the biologic activity of IL-1 including inflammation & cartilage degeneration associated with rheumatoid arthritis

C) Intra articular injection of cortisone:

Indication	- Inflammation of tendon (e.g. tendon achillis) - Used for joints that remain painful despite of general measures
Side effects	- Infection ----- septic arthritis - Rebound pain

C) Surgical treatment:

- Synovectomy
- Arthrodesis
- Joint replacement

There are several kinds of lupus

1- Systemic lupus erythematosus (SLE)

2- Discoid lupus erythematosus: is a chronic skin disorder in which a red, raised rash appears on the face, scalp, or elsewhere. may cause **scarring**

3- Subacute cutaneous lupus erythematosus: appear on sun exposed parts.

Not scarring

4- Drug-induced lupus: presented atypically with systemic features and serositis (associated with anti-histone antibodies) and they typically go away completely when the drug is stopped. **The kidneys and brain are rarely involved.**

5- Neonatal lupus: rare disease in newborn babies of women with SLE, Sjogren's syndrome

Systemic lupus erythematosus (SLE)

Lupus is a Latin for wolf and erythro is a Greek for red (**Red wolf**).

Def.: An **autoimmune** disease characterized by clinical manifestations affecting **multiple organs**, including the skin, joints, kidneys and nervous system

Aetiology:

Altered immunity	Auto-Abs causing damage by cytotoxic effects or Ag-Ab complexes Altered regulating mechanism e.g. decreased T-suppressors
Heredity	HLA B8, DR2 & 3 - 10% have positive family history
Estrogen	Pre-puberty and postmenopausal females of similar incidence to men Exacerbated during early pregnancy and with contraceptive pills
Infection	Virus (nonspecific stimulant of immune response)

Drugs	Anticonvulsants (phenobarbital) Antihypertensives (hydralazine - Methyldopa) Antiarrhythmics (procainamide) Oral contraceptive pills associated with exacerbation
--------------	--

Diagnostic criteria

1. Malar **rash**
2. Discoid **rash**
3. **Photosensitivity**
4. **Painless oral ulcers**
5. **Pleurisy or pericarditis**
6. **Psychosis or seizures**
7. **Peripheral joints arthritis (2 or more)**
8. **Pancytopenia**
9. **Proteinuria or cast**
10. **+ve ANA antibody**
11. **Immunological investigations: +ve anti DNA ab or anti-sm ab**

The diagnosis of SLE is strongly suggested, when a person has 4 or more of these criteria

Clinical picture:-

Type of patient

F : M = 9 : 1

Age: reproductive years, 14 - 40

Bimodal **mortality pattern:-**

- **Early** (within 2 years): active SLE – active nephritis –secondary infection
(steroid use)
- **Late** (> 10 years): inactive SLE – inactive nephritis – atherosclerosis possibly secondary to long-term steroid use

- Type of patient - General
 - Articular (3Ds) - Extra-articular
 - Others

1-General: F A H M

2- Articular:

- Arthritis and arthralgia:

Non-erosive, symmetric; involving 2 or more small or large peripheral joints

In contrast to rheumatoid arthritis, SLE has less morning stiffness and synovial thickening and usually does not lead to joint erosions or destruction

(< 10% of people with SLE will develop deformities of the hands and feet)

- Osteoporosis:

Risk factors: corticosteroids, smoking, early menopause, +ve family history

- Avascular necrosis:

Risk factors: steroids, hyperlipidemia, Raynaud's phenomenon, antiphospholipid antibodies, alcoholism

5- Skin:

Photosensitivity: skin rash as a result of unusual reaction to sunlight

Malar (butterfly) rash: (30%) characterized by erythema, induration and a slight scale

(no scarring as basement membrane is intact)

The discoid lesions: raised, erythematous plaques with adherent scale and occur most commonly on the face, scalp, and neck

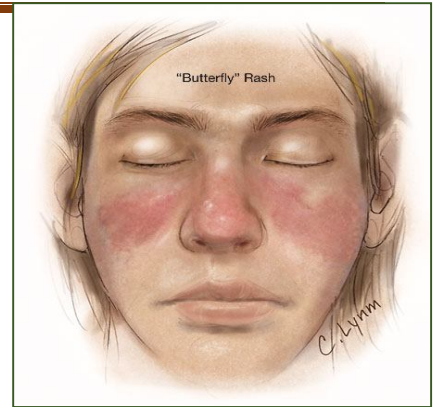
(Late skin pigmentation may occur)

Alopecia: patchy or diffuse alopecia and thin, friable hair may occur during acute SLE flares or as a medication side effect.

(Permanent alopecia can occur)

Oral ulcers: (40%) usually painless and can occur on the hard palate, tongue, buccal mucosa, and gingival surfaces

Vitiligo – telangiectasia – Raynaud's phenomenon



- 6- eye:**
- Conjunctivitis
 - Scleritis ----- repeated attack ----- scleromalacia (blue sclera)
 - Iritis is not common

7- Blood & L.N: Caused by disease itself or by side effects of medications

RBCs:- Anemia of iron deficiency

WBCs:- Leucopenia and thrombocytopenia **Recurrent infection**

(Explained by:- Drugs, Active SLE, renal disease, low serum protein)

Hepatosplenomegaly

Antiphospholipid antibody syndrome (APs)

Investigation

a- Routine:

CBC: Anaemia – bicytopenia or pancytopenia

ESR: markedly elevated

Urinalysis: proteinuria, hematuria, pyuria or red cell casts

KFTs: may be impaired

b- Serological:

Antinuclear antibody test (ANA): most **sensitive**

Anti-ds DNA: most **specific**

Other autoantibody tests:

- Anti-Sm
- Anti-RNP
- Anti-Ro (SSA), anti-La (SSB)
- Anticardiolipin antibody test (see APS)

c- Complement levels: decreased

d- Immunoglobulin: increased

- e- **LE cells:** leukocyte with large inclusion body
(Ag-Ab complex)
- f- **Biopsy:** Skin biopsy - Kidney biopsy



Treatment

1- Modifications of lifestyle:

- Use of sunscreen
- Regular exercise, a healthy diet and sufficient rest.
- Avoidance of estrogens

2- Mild-to-moderate disease (no major organ involvement)

Combination of therapies that include:-

NSAIDs

Corticosteroids (< 10 mg/d)

Antimalarial agent such as hydroxychloroquine

- **NSAIDs:** for mild **arthritis** and arthralgias, SLE-related **fevers** and **serositis**
- **Antimalarial:** For **mild arthritis** and arthralgias, **skin disease** and fatigue also to prevent more serious flares of disease.
- **Topical steroids:** for rash

3- Severe disease (major organ involvement: glomerulonephritis, pneumonitis, vasculitis, neurological disease, myositis, cytopenias)

- **High doses of corticosteroids:** the usual initial dose of prednisone is in the range of 0.5 to 1.0 mg/kg per day
- **Other immunosuppressive:** include cyclophosphamide, methotrexate, azathioprine and mycophenolate
- **Intravenous immunoglobulins** may be used to control SLE with vasculitis.
- **Plasmapheresis:** used during disease activity (nephritis)

Drugs:-

Drug	Side effects
NSAIDs	Peptic ulcers - bleeding - increased liver enzymes - impaired renal function - HTN - edema and aseptic meningitis
Corticosteroids	HTN, DM, hyperlipidemia, avascular necrosis, osteoporosis, Myopathy, cataract, weight gain, adrenal insufficiency and infection
Chloroquine	Macular damage, rash, CNS effects and Myopathy
Methotrexate	BM suppression, cirrhosis, pulmonary infiltrates or fibrosis and lymphoproliferative disorders
Azathioprine	BM suppression, hepatotoxicity, lymphoproliferative
Cyclophosphamide	BM suppression, myeloproliferative disorders, malignancy, hemorrhage cystitis, bladder cancer, sterility and SIADH

Antiphospholipid syndrome

Def.: Multisystem vasculopathy manifested by recurrent **thromboembolic** events, spontaneous **abortions** and **thrombocytopenia**

Types:

1- Primary APS: no detectable causes

2- Secondary APS develops in: SLE, other connective tissue diseases, malignancy, drugs (hydralazine, procainamide, phenytone, interferon, quinidine), infections (HIV, hepatitis C, TB, infectious mononucleosis)

Clinical picture

Venous or arterial occlusion

- Venous occlusion: DVT, P. embolism, renal and retinal vein thrombosis
- Arterial occlusion – stroke, TIA, multi-infarct dementia, chorea, myocardial infarction, valvular incompetence, limb ischemia

Recurrent spontaneous abortions

Haematological: thrombocytopenia, hemolytic anemia, neutropenia

Skin: Livedo reticularis (classical lesion), purpura, leg ulcers, and gangrene

Catastrophic APS: Fatal condition with sepsis, ARDS, malignant HTN, multi-organ infraction

Serology:- Lupus anticoagulant or anticardiolipin antibody



Treatment

Thrombosis: lifelong anticoagulation with warfarin (INR = 2.5-3.5)

Recurrent fetal loss: aspirin, heparin, +/- steroids

Catastrophic APS: high-dose steroids, anticoagulant, cyclophosphamide or plasmapheresis

Sero-negative arthritis (spondylo)

1. Ankylosing spondylitis
2. Reactive arthritis
3. Psoriatic arthritis
4. Enteropathic arthritis

Ankylosing Spondylitis (AS)

Def.: type of the **spondylo-arthropathies** characterized by **sacroilitis**, **spondylitis** and marked **fibrosis**

Incidence

- 0.2% of general population
- M:F = 3:1 (females have milder disease)
- **HLA B27** in 90% of patients (9% in the general population)
- Association: **Prostatitis** (100%) ± ocular affection

Pathophysiology:

Enthesitis: inflammation of ligament at the site of attachment then osteopenia then erosion then ossification

Clinical picture

A) Articular

1- Axial

Bilateral sacroilitis:

Pain: Mid-low back **stiffness**, pain at rest, partially improved by movement
± persistent buttock pain

On examination: painful sacroiliac joint

Spinal affection

Spinal restriction: Lumbar-thoracic-cervical spine in flexion-extension-rotation

On examination:

Postural changes: increased dorsal kyphosis, decreased lumbar lordosis, forward protrusion of cervical spine (**flexion**)

Increased **occiput-to-wall** distance (flexion attitude)

Decreased chest wall **expansion**

Decreased **Schröber** test (decreased forward flexion of lumbar spine)

2- Peripheral

Asymmetrical large joint peripheral arthritis, mainly lower limbs with **centrifugal** spread

Spontaneous remissions and relapses

B) Extra-articular manifestations

Genito-urinary: Prostatitis (100%)

Eye: Acute anterior uvetitis (25-30% patients)

Heart: aortitis, aortic regurgitation, pericarditis, heart block, heart failure (rare)

Kidney: amyloidosis and IgA nephropathy

Pulmonary: apical fibrosis (rare)

GI: IBDs (UC)

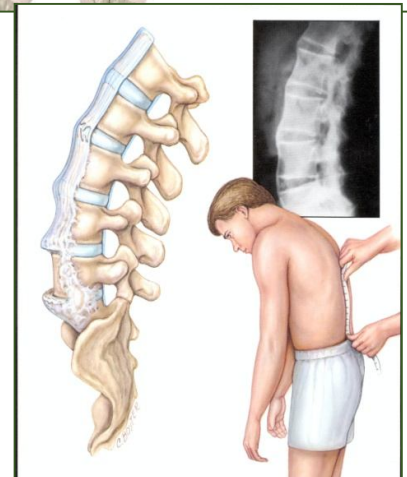
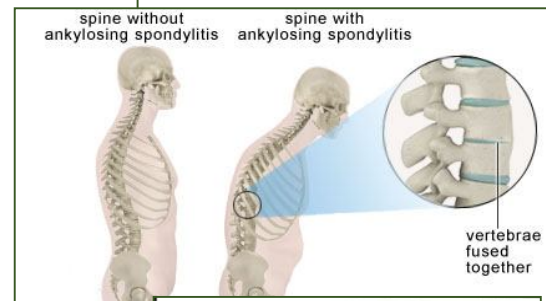
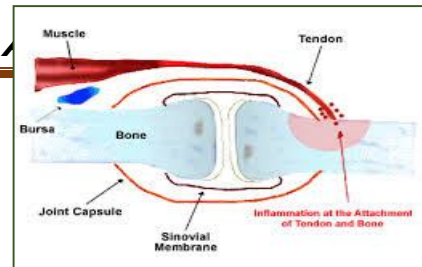
Neurology: cauda equine syndrome (rare) – atlantoaxial subluxation

5 As: anterior uvetitis, aortitis, amyloidosis, IgA nephropathy and apical fibrosis

Investigations

X-ray:

Sacroiliac joint: Early: pseudo-widening of the joint due to erosion
Late: joint sclerosis ----- bony fusion



Spine:

Early: **Square-shaped vertebra** = due to erosion and sclerosis of the its corners

Late: Ossification of the outer fibers of annulus fibrosis (**bridging syndesmophytes**) –

Ossification of the longitudinal ligament producing a **bamboo spine or Dagger**



Laboratory tests:

- **Rheumatoid factor** = negative
- **Elevated ESR & C-reactive protein**

Prognosis

- Good in female and onset after age 40
- Early hip disease may lead to severe disability

Treatment

1- Physiotherapy:

Exercise (e.g. swimming) – Postural and deep breathing exercises to prevent fusion in poor posture and disability.

2- Pharmacological therapy:

- NSAIDs: do not alter natural history
- DMARDs for peripheral arthritis (sulfasalazine, methotrexate)
- **Infliximab** for axial involvement
- Symptomatic treatment: as for extra-articular manifestations

3- Surgery: hip replacement, vertebral osteotomy for marked deformity

Reactive arthritis (Reiter's)

Def.: Type of arthritis following an infection (e.g. rheumatic fever, Reiter's)

Incidence: - 90% of patients are **male** -age = **20-40**

- Positive for **HLA B27** (axial > peripheral)

Aetiology: Following an infectious episode either involving the GI or GU tract

GI: Shigella, Salmonella, Campylobacter, Yersinia species

GU: Chlamydia, Mycoplasma species

Course of the diseases: Acute onset - 1-4 weeks post-infection
Lasts week to years (1/3 chronicity)
Usually recurrent but spinal form persists

Clinical picture (**AUC: arthritis, urethritis and conjunctivitis**)

Articular

- Peripheral arthritis of asymmetrical pattern
- Spondylitis (asymmetrical pattern)
- Enthesitis of **LL** (planter fascitis, Achilles tendonitis)
- **UL** (Sausage digits)

Sausage digits are characteristic of reactive and psoriatic arthritis

Others

- **Eye:** Iritis
- **GI:** oral ulcers, diarrhea
- **Keratoderma blennorrhagica:** hyperkeratotic skin lesions on palms and soles
- **Balanitis:** small, shallow, painless ulcers of glans penis and urethritis.



Investigation

CBC: normocytic normochromic anaemia and leukocytosis

ESR: elevated

Synovial fluid cultures: negative (sterile)

X-ray: according to the affected joint (may be like Ank. S)

Treatment

- **Antibodies** :- if there is documented infection

- **Joint Therapy**

NSAIDs, physical therapy, home exercise

Intra-articular **steroid** injection (in **resistant** cases)

Corticosteroid, sulfasalazine, methotrexate (**for peripheral joints only**)

- **Symptomatic:** Topical steroid for the eye = skin lesion has no specific treatment

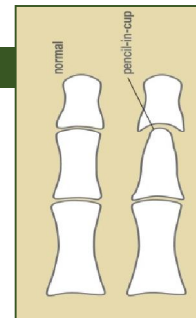
Psoriatic arthritis

- Psoriasis affects 1% of population
- Arthropathy in 10% of patients with psoriasis
- 15-20% of patients will develop joint disease before skin lesions

Clinical picture:

Skin and nail changes are typical findings

- Well-demarcated erythematous plaques with silvery scale
- Nail:- pitting, ridging, discolouration, hyperkeratosis or onycholysis



Joints: 5 general patterns

- Arthritis of **DIP** joints with nail changes
- **Destructive** arthritis (5%)
- Symmetrical **polyarthritis** (similar to **RA**)
- **Sacroilitis** and **spondylitis** (usually older, male patients similar to **Ank. Sp.**)
- Asymmetrical (most **common**)

Other features (complications)

Eye: conjunctivitis, iritis

Heart: aortic insufficiency

Lung: apical lung fibrosis

Neurological: peripheral nervous system – cauda equine

X-ray:

- Floating syndesmophytes
- **Pencil and cup** appearance at IP joints
- Osteolysis, periostitis



Treatment:

Treatment of the skin disease: steroid cream, salicylic/retinoic acid, tar

Severe disease with erosive arthritis

- NSAIDs
- Intra-articular steroids if NSAIDs fail to reduce synovitis and pain
- DMARDS: methotrexate, sulfasalazine, cyclosporine, gold, chloroquine, azathioprine, and TNF inhibitors (infliximab)

Arthritis with IBD

- Particular manifestations of ulcerative colitis and/or Crohn's disease include
 - 1- Peripheral arthritis (large joint, asymmetrical)
 - 2- Spondylitis
 - 3- Hypertrophic osteoarthropathy
- Arthralgia, myalgia, osteoporosis and aseptic necrosis of bone secondary to glucocorticoid **treatment** of the bowel inflammation

Scleroderma

Progressive systemic sclerosing (PSS)

Def: Generalized disorder of connective tissue characterized by **fibrosis** and degenerative changes in **blood vessels**, **visceral** organ and **skin**

- No inflammation
- Clinical hallmarks of PSS are tight skin and Raynaud's phenomenon
- Diagnosis made on clinical grounds (no specific Abs 100%)

Incidence:

- F:M = 3-4:1
- Incidence peaks in 5th and 6th decade (may be earlier)
- Associated with **HLA DRI, DR3, DR5**
- May associated **environmental** factors

Pathogenesis: - *Fibroses and degenerative changes in skin and viscera:- Collagen deposition leading to atrophy and fibrosis*
Blood vessels:- intimal proliferation and medial degeneration progressive obliteration → secondary fibrosis of tissue.

Clinical picture (cutaneous - extracutaneous)

A) Cutaneous

Hand:

- Bilateral symmetrical swelling of fingers, hands and feet leading to skin tightening (**scelerodactely**)
- Initial phase characterized by painless pitting edema, which on resolution leaves **thick, tight** skin

Characteristic face: mask, fish mouth, beak nose, radial peri-oral furrows

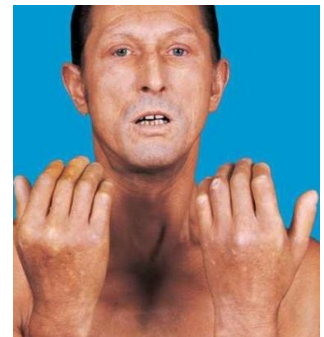
Other skin changes: atrophy, ulcerations, hypo- and hyperpigmentation, telangiectasias, calcinosis, periungual erythema, pruritus

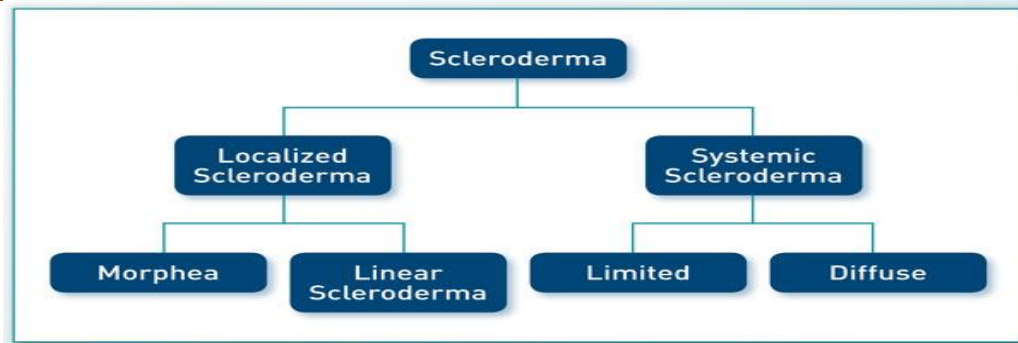
Raynaud's phenomenon

Clinically presents as episodes (minutes or hours) of blanching and/or cyanosis of digits followed by erythema, tingling and pain

Due to Vaso-spasm after cold exposure or emotional stress If severe, can result in infarction of tissue at fingertips → digital pitting scars, frank gangrene or auto-amputation of the fingers or toes.

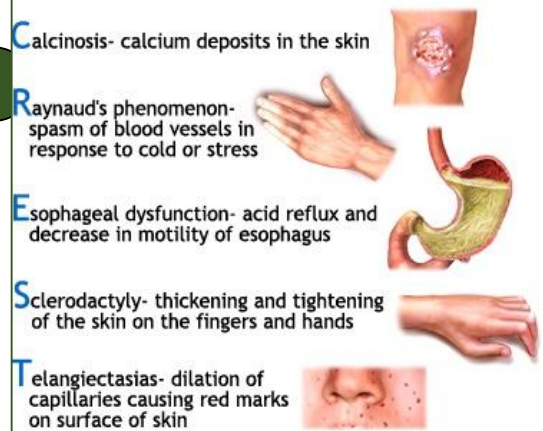
Scleroderma is the most common cause of secondary Raynaud's phenomenon





Localized (no internal organs) Children and young adults		Generalized (systemic sclerosis)	
Morphea	Linear	Limited	Diffuse
Hard oval Patches on the skin	Line of Thickening	- Hands, face & neck - 3 rd to 4 th decade - + Pul. Hypertension	- Widespread skin lesion - Early visceral: (renal, pulmonary)

CREST



B) Extra-cutaneous

GI tract (~90%) rigidity leads to hypo- motility

- Distal esophageal hypo-motility:- **dysphagia** in substernal region
- Lower esophageal sphincter dysfunction:- **GERD**
- Small bowel hypo-motility:- bacterial overgrowth, **malabsorption**, weigh loss
- Large intestine hypo-motility may cause **constipation**

Pathognomonic radiographic finding on barium contrast studies.

Kidneys

- *Scleroderma renal crisi*: (10-15%) may lead to malignant **HTN**, **oliguria** and microangiopathic hemolytic anemia
- *Urine abnormalities*: Mild **proteinuria**, creatinine elevation and/or **HTN** (commonest)

Lungs:

- *Pleural*: pleurisy and pleural effusions
- *Lung*: interstitial fibrosis – carcinoma
- *Vascular*: pulmonary HTN
- *Extra thoracic*: tight skin may lead to restrictive hypoventilation.

CVS:

- *Peri*: pericarditis, pericardial effusion or constrictive.
- *Myo*: left ventricular dysfunction, arrhythmias
- *Endo*: MR – TR

Musculoskeletal:

- Joint: poly-**arthralgia** or -arthritis (both small and large joints)
- Muscle: **Myalgia** or myositis.
- Bones: resorbed with subcutaneous calcifications (**calcinosis**)
- Resorption of **distal tufts**: radiological finding

Diagnostic criteria:

1 major or ≥ 2 minor of the following

Major criterion: proximal scleroderma

Minor criteria:

- Sclerodactyly
- Digital pitting scars or loss of finger pad,
- Bi-basilar Pulmonary fibrosis

Endocrine: may have hypothyroidism

Investigation:

CBC & ESR: - Anaemia may be haemolytic
- Elevated ESR

Serology

- Anti-scl 70
- Anti-topoisomerase 1: specific but not sensitive for systemic sclerosis
- Anti-centromere: for diagnosis of CREST
- Others: ANA – Rh F. – LE cells

Images

- Hand: calcinosis of the fingers – resorption of distal tufts
- Chest: IPF
- GI: barium contrast



Biopsy: from the skin

Treatment

General: Avoidance of exposure to cold

Specific:

Penicillamine of little value

Steroids: in early phases

Others: methotrexate/cyclosporine

Symptomatic treatment

GERD: proton pump inhibitors

Intestinal bacterial overgrowth: broad-spectrum antibiotics (tetracycline, flagyl)

Raynaud's: Ca blockers, Vasodilators, Nitroglycerin cream, systemic PGE2 inhibitors

Renal disease or HTN: ACE inhibitors

Myositis or pericarditis: steroids.

Vasculitis

Def:- Inflammation of the wall of blood vessels including veins (phlebitis) arteries (arteritis) and capillaries

Classification

- Large vessel vasculitis:-**
- Takayasu arteritis
 - Giant cell (temporal) arteritis
- Medium vessel vasculitis**
- Polyarteritis nodosa (PAN)
 - Wegener's granulomatosis
 - Kawasaki disease
 - Isolated CNS vasculitis

Small vessel vasculitis

<u>Non-ACNA-associated</u>	<u>ANCA-associated</u>
- Predominantly cutaneous vasculitis (allergic vasculitis) - Henoch-Schönlein purpura - Essential cryoglobulinemic vasculitis	- Wegener's granulomatosis - Churg-Strauss vasculitis - Microscopic polyangitis

Others:- Buerger's disease – Behcet's disease – Vasculitis mimicry

Clinical picture

A- Common (nonspecific)*

Constitutional: fatigue, weakness, fever, arthralgias, abdominal pain and loss of weight

Systemic: Hypertension, renal insufficiency and neurological dysfunction

Superficial ischaemia: e.g. fingers ulcers, palpable purpura

- Vasculitis is a rare disorder
- Several organs may be affected
- C/P depends on which vessels are affected



B- Specific features:- depends on which vessels are affected (** C/P page 62)

Diagnosis:

1) Laboratory:

- Basic lab. Tests: CBC, ESR, urine and stool analysis, KFTs and LFTs.
- For DD: Muscle enzyme, hepatitis serology
- Specific tests: Antinuclear antibody (ANA), Antineutrophil cytoplasmic antibody (ANCA) and **complement** levels (low level in mixed cryoglobulinemia, HCV, and SLE but not most other vasculitis)

2) Image:

- Duplex: non invasive
- Arteriography: helpful in large and medium-sized vasculitis but not in small vessel vasculitis (may show aneurysms, occlusions, and vascular wall abnormalities)

3) Systemic:

- **Neurological:** Electromyography (EMG)
- **Lung:** X-ray
- **C.V.S.:** ECG – Echo
- **Abd.:** Ultrasound – C-tscan

4) Tissue biopsy: This is the gold standard of diagnosis (**invasive**)

Treatment

- Treatment of the underlying **cause**
- **Steroids** (e.g. methylprednisolone)
- **NSAIDs**:- in mild forms of some vasculitis, such as **Kawasaki** disease
- **Immunosuppressants**:- cyclophosphamide and azathioprine
- **Others**: anti TNF (Remicade, Enbrel) and rituximab (Rituxan)
- **Exercise**:- Regular aerobic exercises, such as walking, can help prevent bone loss, high blood pressure and diabetes

** B- Specific types

Large vessel vasculitis

Giant cell (temporal) arteritis

- **Granulomatous** vasculitis of both large and medium vessels of cranial arteritis
- More common in **women** = can lead to **blindness** (20-25%)
- Tongue and jaw claudication

At least 3 out of 5 criteria:

- Age at onset ≥ 50 y.
- New onset **headache** with localized tenderness
- Temporal artery **tenderness** or decreased pulsation
- Elevated **ESR** ≥ 50 mm/h
- Temporal artery biopsy **granulomatous** inflammation, with **giant** cells

Medium vessel vasculitis

Polyarteritis nodosa (PAN):- Systemic necrotizing vasculitis and aneurysm formation affecting both medium and small arteritis

Clinical picture:

- **General**: as usual (*page 61)
- **Joints**: arthralgia and arthritis usually early in course
- **Kidney**: aneurismal dilation (not glomerulonephritis) – **HTN** (25% of patients)
- **Peripheral nervous**: may be mononeuritis multiplex
- **GIT**: abdominal pain, GIT bleeding, ischemic bowel, transaminase elevation
- **Skin**: palpable purpura, ulceration and digital tip infarct
- **Heart**: Myocarditis (tachycardia) – MI (coronary arteritis) – CHF

Wegener's granulomatosis: Nose + Lung + Kidney

Systemic vasculitis of medium and small venules or arterioles

- **Granulomatous** inflammation of the Lung and **Glomerulonephritis**
- Most common cause of **saddle nose** deformity in USA
- Almost all patients with had ANCA

Kawasaki disease: children IHDs

- Usually in **children**, prominently affecting the **coronary** arteritis
- Associated with lymph node enlargement

Small vessel vasculitis

Churg-Strauss arteritis:

Affecting medium and small vessels with vascular and extra vascular granulomatosis
Triad of allergic **rhinitis**, **asthma** and systemic **vasculitis**

Henoch-Schönlein purpura (see blood)

Systemic vasculitis due to tissue deposition of IgA
This is the most common vasculitis in children

Essential cryoglobulinemic vasculitis

- Most often due to HCV
- Affecting capillaries, venules or arterioles

Vasculitis mimicry

- Cholesterol emboli
- Atrial myxoma

Behcet's disease

Inflammatory disorders of an unknown aetiology

Epidemiology:- - Common in Turkey, Iran & Japan
- With **HLA-B51**

C/P: Diagnostic criteria:-

Recurrent oral ulcers + 2 of the following

- Genital ulcer
- Defined eye disease (Ant. Or post. Uveitis)
- Skin Lesion as erythema nodosum
- Positive pathergy test

Others:-

- Mono or oligo arthritis
- C.N.S. (as M.S.)
- GIT manifestation
- Pulmonary lesion
- Renal lesion

All manifestation are self limited except uveitis which may cause blindness

Pathergy reaction:- *is highly specific, skin injury by a needle prick for example leads to papule or pustule formation within 24-48 hrs.*



TTT.:

- Steroid & immune suppressive:- for eye & neurological complication.
- Colchicin for Joint & skin manifestation.
- Topical steroid for oral & genital ulcers.

Polymyositis (PMY) or dermatomyositis (DMY)

PMY	DMY
CD8 cell-mediated	Mediated by B cell and CD4
Adults	Children and adults
Equal	F > M

Classification and types

1. PMY or DMY
2. Juvenile DMY (with vasculitis)
3. PMY/DMY with malignancy
4. PMY/DMY with CT disease
5. Amyopathic DMY
6. Inclusion body myositis (IBM)

Clinical picture

1- Dermatological lesions:

Gottron's papules: pink, flat-topped papules over the dorsal surface of IPL

Gottron's sign: erythematous smooth or scaly patches over the dorsal surface of IPJ or MPJ, elbow, knees or medial malleoli

Gottron's papules and sign are pathognomonic of DMY (70% of cases)

Heliotrope (purple) rash over the eyelids: usually with edema

Shawl sign: erythematous rash over neck, upper chest, and shoulders

Clacification (late): localized (fingers) or generalized

2- Muscular lesions

- Progressive symmetrical proximal muscle **weakness**
- Signs of **myositis**: pain and tenderness

3- Others

Cardiac: dysrhythmias, congestive HF, HB, V.hypertrophy or pericarditis

GI: Dysphagia (oropharyngeal or lower esophageal)

Pulmonary: weakness of muscles, IPF or aspiration infection

Diagnosis

- **Muscle enzyme:** increased CK, aldolase, LDH, transaminases (AST)
- **EMG:** short motor units with insertional irritability
- **Muscle biopsy:** perivascular inflammation and atrophy
- **Autoantibodies:** ANA, anti-jo-1, anti-Mi-2, myositis-specific Ab (**MSAs**)
- **Assessment of organ affection:** ECG, Chest X-ray, swallowing study
- **Malignancy surveillance:** Chest X-ray, abdominal and pelvic ultrasound, stool occult blood, Pap smear, mammogram

Treatment

- High dose **corticosteroid** (1-2 mg/kg/day) and slow taper
- **Immunosuppressive:** azathioprine, methotrexate and cyclophosphamide
- **IV Ig:** intravenous immunoglobulin for DMY
- **Physiotherapy**

Idiopathic inflammatory Myopathy

- Proximal limb and neck weakness (with or without pain)
- Caused by: collagen – malignancies – idiopathic



Mixed connective tissue disorder (MCTD)

Overlap syndrome

Def.: Combination of RA, SLE, scleroderma and polymyositis

Incidence: Common in females at the 4th decade

Clinical picture: as RA, SLE, scleroderma and/or polymyositis

Investigations:

- Anti-ribonucleoprotein Ab (**anti-RNP**) "speckled ANA fluorescence"
- Anti-ds-DNA, Sm and histones: negatives

Sjögren's syndrome

Def.: Cell-mediated infiltration and destruction of salivary and lacrimal glands

Types:-

1- **Primary** (isolated)

2- **Secondary** (on top of RA, SLE, DMY or HIV)



"sicca complex": dry eyes (keratoconjunctivitis sicca), dry mouth (xerostomia)

Clinical picture:

Eye: Burning/dry/painful eye relieved by tears – Blepharitis

Oral: Dry mouth-difficulty swallowing food without drinking – Dental caries – erythema of mucosa – oral candidiasis – angular cheilitis

Systemic: arthralgias/arthritis, subclinical diffuse interstitial lung disease, renal disease, palpable purpura, systemic vasculitis, lymphoma (high risk for NHL)

Diagnosis (SSASSS)

S: Schirmer test (assess tear flow)

S: Slit lamp exam with Rose-Bengal stain

A: Autoantibodies (anti-Ro and-La)

S: Salivary flow measurement

S: Sialography

S: Salivary gland biopsy (gold standard)



Treatment

Eye: - artificial tears or surgical TTT

- treatment of complication as staphylococcal blepharitis (commonest)

Oral: - Good dental hygiene

- Adequate hydration

- Topical nystain/clotrimazole x 4-6 weeks for oral candidiasis

Hydroxychloroquine, corticosteroids or immunosuppressive agents for severe systemic involvement

<<onion cooking with no tears>> usual housewife complaints

Septic arthritis

Def.: Suppurative infection of the joint usually acute
mono-arthritis permanent joint damage can occur

Aetiology:



Source and rout of infection	Predisposing factors
- Haematogenous spread (adults) - Direct: osteomyelitis (children) - After trauma - Iatrogenic: arthrocentesis	- Extra-articular infection (UTI - skin) - Chronic debilitating illness (DM - cancer) - Previous joint damage (OA – RA - prosthetic) - Low immune status

Common organism

Age related	• Infant: H. influenza • Children: S. pneumonia • Young adults: N. gonorrhoeae: (75% of all cases) • All ages: S. aureus (rapidly destructive)
Special situation	• Debilitating patients: Gram negatives • Patients with sickle cell: Salmonella

Clinical picture

- Bacteremia: fever and malaise
- The affected joint: swollen, warm, painful, with marked tenderness

Gonococcal triad:

1. Migratory arthritis
2. Tenosynovitis
3. Maculopapulovesicular skin rash

Diagnosis:

- Synovial fluid
 - * Opaque * PMNs > 85%
 - * Gram stain * Culture and sensitivity
- Other cultures: blood and urine culture
- Synovial biopsy: for undiagnosed cases
- Pain X-ray: for exclusion of osteomyelitis

In gonococcal infection:-

endocervical, urethral and oropharyngeal cultures may be positive

Treatment

General support:

Symptomatic treatment:

- Pain killer
- Firstly immobilization then physiotherapy

Specific

Antibiotics: Start IV antibiotics empirically as 3rd generation cephalosporin + penicillinase resistant synthetic penicillin (e.g. ceftriaxone + cloxacillin)

Surgical drainage: indicated in

- Failure of medical treatment after 3 days
- Affection of hip joint
- Daily joint aspirations until culture sterile



Intra-articular steroids are contraindicated

Fibromyalgia

Def.: chronic diffuse pain with characteristic tenderness

Incidence: - F : M $\geq 3 : 1$

- Ages **25 to 45**, some adolescents
- **2-5% in general population** (overlaps with chronic fatigue syndrome)
- Strongly associated with **psychiatric** illness

Clinical features

- Wide-spread **aching** adolescents
- Aggravated by **physical** activity, poor sleep and emotional stress
- Joint examination: usually **normal**
- Hyperalgesia or paresthesias
- **Associated** with irritable bowel syndrome, migraines, tension headaches, obesity, depression and anxiety

Investigation: typically **normal**

Treatment

Non pharmacological

- Patient **reassurance**: disease is benign, non-deforming and does not progress
- **Biofeedback**, meditation, acupuncture, physiotherapy may be helpful
- **Exercise** program (walking, aquatic exercises)
- **Support** the back and the neck
- **Psychotherapy**

Pharmacological

- **NSAIDs** if pain interferes with sleep
- **Antidepressants**

Diagnosis:-

- 3 months history of pain
- **Exclusion** of other causes, e.g. polymyositis, polymyalgia rheumatic, Endocrine disorders.

Polymyalgia rheumatica

Def.: Major pain and stiffness of the proximal extremities

Associated with giant cell arteritis

Age > 50 ----- F : M = 2 : 1

Clinical features

- **Constitutional** symptoms
- **Stiffness** of **proximal** muscles and joints (neck, hip, shoulder and thighs)
- Tender muscles but **no weakness** or atrophy

Investigations

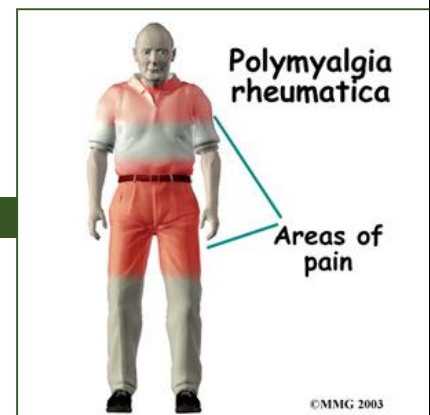
- Anemia
- ESR: elevated
- CK: normal

Treatment

- **Symptomatic** therapy
- **Steroid** therapy:- Small doses 15-20 mg taper monitoring ESR and symptoms

Diagnostic criteria

- Age > 50 y
- > 2 muscle groups
- ≥ 2 week duration
- Increased ESR
- Rapid response to corticosteroids
- Exclusion of others (RA, SLE, PAN or malignancy)



Rheumatology By DR| M. A / I AM

Hypersensitivity		
Name	Pathogenesis	CAP
1-immediate Atopic \ anaphylactic Rapid (few seconds)	Provoked by re- exposure to a specific type of antigen (allergen) Ag-Ab=Mast cell releasing IgE:- - vasodilation - smooth-muscle contraction By:- - Ingestion - Inhalation - Injection - direct contact	The reaction may be local or systemic <u>Systemic:-</u> Severe VD = may death (anaphylactic shock) <u>Local</u> (Atopy) - Bronchial asthma (Extrinsic) - Allergic rhinitis (by fever) - Angioedema TTT:- adrenaline - anti-histaminic - steroid
2- cytotoxic reaction antibody-dependent takes hours to a day	Intrinsic "self": part of the patient's cell Extrinsic: absorbed onto the cells during exposure to some foreign antigen, possibly as part of infection with a pathogen Ag-Ab (IgM/IgG) = fixation of Complement and then lysis (cytotoxic) of the cells May be induced by hapten (incomplete Ag) as drugs (penicillin - sulpha) <i>Another form of type 2 hypersensitivity is called antibody-dependent cell-mediated cytotoxicity (ADCC)</i>	- Autoimmune hemolytic anaemia - Goodpasture's syndrome
3- immune complex take hours, days, or even weeks	Immune complexes are deposited in vessel walls and induce an inflammatory response (vascular damage)	Arthus: localized form at the site of Ag injection (vasculitis) Serum sickness: usually after serum administration may presented with urticaria , laryngeal oedema , organ affection (GN - myocarditis) - Rheumatoid arthritis - Serum sickness - Immune complex glomerulonephritis
4- cell-mediated (delayed-type hypersensitivity; DTH)	It is cell-mediated response - takes two - three days	- Contact dermatitis - Tuberculin test Chronic transplant rejection
5- stimulatory	Antibodies bind to the cell surface receptors , which either stimulate or inhibit the cell action	- Graves disease - Myasthenia gravis

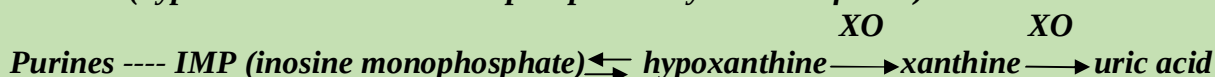
(There is also a type 6 hypersensitivity reaction in which natural killer cells lyse cells that have been coated in antibody and this reaction is thought to be implicated with certain autoimmune diseases, tumor rejection & parasite rejection)

Gout

Definition: It is a clinical syndrome manifested by:

- **Hyperuricemia** > 7 in M (N: 2.5 – 7 mg/dl) > 6 in F
- Deposition of uric acid in the **tissue** (tophi)
- Deposition of uric acid in the **joint** (Gout arthritis)
- Deposition of uric acid in the **kidney** (Gouty nephropathy)

HGPRT (hypoxanthine – Guanine – phosphoribosyl - Transferase)



Aetiology:

Increased Production (metabolic gout)		Decreased Excretion (renal Gout)	
1ry	2ry	1ry	2ry: 2A + 2D
Enzymatic defect e.g: HGPRT	- leukemia - lymphoma - sarcoidosis	Idiopathic (Isolated tubular defect)	- Acute renal failure - Acidosis - Dehydration ----- ↓ renal flow - Drugs: e.g. thiazide, frusemide

N.B.: Causes of hypourcemia:

- Pregnancy ----- GFR↑↑ - Fanconi syndrome – Iatrogenic: allopurinol

Pathology:

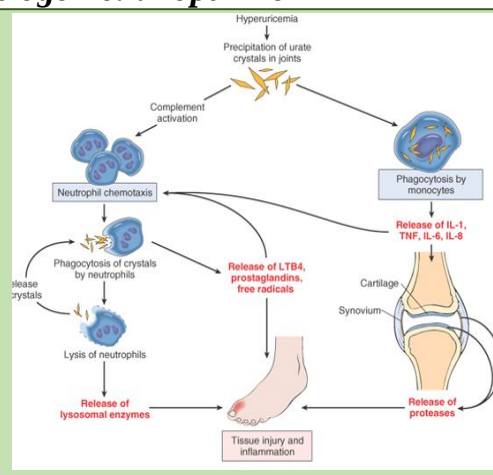
1- Acute gouty arthritis:

Uric acid in itself is not irritant to joint but when **urate crystals** deposited in joints ----- phagocytosed by **macrophage** ----- release of **lysosomal enzymes** which produce inflammatory reaction ----- acute gouty arthritis

2- Chronic gout:

Deposition of uric acid in:

- Joint: chronic erosive arthropathy
- Kidney: gouty nephropathy
- Tissue: Tophi



Clinical picture

M > F 40-50 y.

1- Asymptomatic hyperuricemia: > 90% of hyperuricemic patients

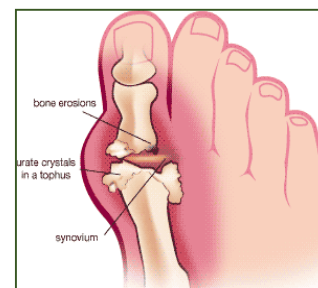
2- Symptomatic: A- Acute gouty arthritis B- Chronic gout

Acute gouty arthritis: 3D

Ppt factors: trauma, infection, alcohol

Distribution: - Monoarthritis

- Usually in the first **MTP** joint (of the big toe)



Description: hotness, redness, tenderness, swollen & limitation of movement especially to big toe

Deformity: No (Non-erosive)



B- Chronic gout:

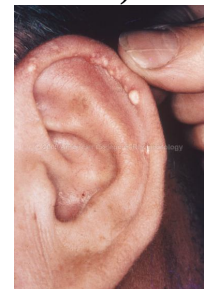
- 1-Arthritis:**
- Polyarthritis
 - Asymmetrical
 - Erosive
 - Remission & exacerbation
 - Deformity: may be

2- Gouty nephropathy:

- Precipitation of uric acid into renal tubules ---- **ARF or CRF**
- Precipitation of uric acid in renal interstitium ----- **chronic interstitial nephropathy** ----- CRF
- Precipitation of uric acid in urinary tract ----- **urate stones** (Hematuria-UTI)

3- Tophi:

- Occurs with severe hyperuricemia
- Ppt of Na urate SC especially around the joints & ear lobule.
- May ulcerate & discharge chalky paste material



Investigations:

1. Uric acid (N= 2.5 – 7 mg%) > 7 mg% in M : > 6 mg% in F.
2. X-ray: punched out lesion
3. Biopsy from tophi
4. Aspiration of synovial fluid ----- urate crystals
5. U/S kidney

Treatment:

A- Asymptomatic hyperuricemia:

- No treatment except with:**
- +ve family history
 - Uric acid > 11 mg%
 - Excessive Excretion of uric acid in urine

B- Acute gouty arthritis:

1- NSAIDs:

- Indomethacine: 75 mg & then 50 mg/6h
- Diclofenac: 75 mg & then 50 mg/6h

2- Colchicine:

1-2 mg then 0.5 mg/6h (maximum does 6 mg)

3- Short term cortisone

C- Chronic gout: (hypouricemic drug)

- Indication:**
- Recurrent acute gout
 - Tophi
 - Joint deformity
 - Nephropathy

Colchicine

Mech:- mitosis inhibiting function

Uses:-

- Acute Gout
- chondritis
- Behcet,s
- Skin lesion
- FMF (prophylaxis)
- aphthous stomatitis
- with others in pericarditis
- Amyloidosis.
- Sarcoidosis
- Q; Cirrhosis

S/E: GITD - BM suppression (Leucopenia) - PN

*** Allopurinol (zyloric):**

Dose: 100 – 300 mg/d

Mech: xanthine oxidase inhibitor

S/E: fever, diarrhea, allergy, BM depression

*** Uricosuric drugs (probenecid):**

Dose: 0.5 – 1 gm/12h

Used with **alkalinization** of urine

N.B.: It is important to drink plenty of fluids with anti gout drugs

Diet in Gout:

- There is no need for severe dietary restriction
- Avoid excessive meat intake & alcohol

Pseudo-gout

(chondrocalcinosis)

Definition: Deposition of **Ca pyrophosphate** crystals in cartilage

Aetiology: - Idiopathic

- Some metabolic diseases: hypercalcemia, DM, CRF, hemochromatosis

Clinical picture: M = F

Mono arthritis especially in the knee

Investigations:

1. X-ray: cartilage calcification
2. Ca-pyrophosphate crystals in synovial fluid
3. ESR ↑

Treatment: NSAID - Intra-articular cortisone

Pseudo-pseudo Gout:-

- Hydroxy-appatite arthropathy (Crystal arthropathy)
- F > M- shoulder joint is the commonest site

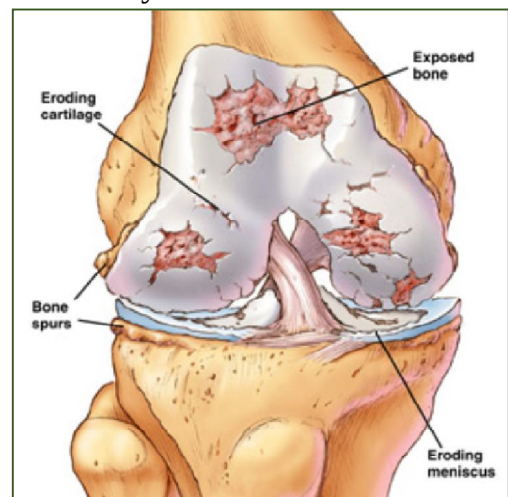
Osteo-arthritis (OA)

Def.: Degenerative disorder of articular cartilage -It is the **commonest** arthropathy

Usually age-related: **35% of 30** years olds – **85% of 80** years olds

Pathology (cartilage = bone = synovium)

1. Degeneration of the articular **cartilage** due to local biomechanical factors and release of proteolytic and collagenolytic enzymes
2. Abnormal local **bone** metabolism
 - Sub-chondral sclerosis
 - Bone grows beyond joint margin = osteophytes (**spurs**)
3. **Synovitis** is secondary to cartilage damage



Aetiology and classification

A- Primary (idiopathic)	B- Secondary
- Unknown (common) - Usually generalized and affecting the DIP joints (nodal or non-nodal)	- Post-traumatic or mechanical - Post-inflammatory (e.g. RA) or infectious - Skeletal disorders (e.g. scoliosis) - Endocrine disorders (acromegaly, hyperparathyroidism, hyperthyroidism) - Metabolic disorders: gout, pseudogout, hemochromatosis, Wilson's - Neuropathic (as Charcot joints) - Atypical joint trauma due to loss of sense (e.g. diabetes, syphilis) - Avascular necrosis (e.g. fractures, steroids, alcohol, gout, sickle cell) - Other (e.g. congenital malformation)
<u>Clinical picture (pain)</u> <i>Cartilage contains no pain receptors; sensation likely results from inflammatory mediators</i>	
<u>Pain:-</u> ▪ Insidious and gradually progressive ▪ Flare-ups and remissions may occur ▪ Increased by movement and relieved with rest ▪ Short duration of stiffness (< 1/2 hr) after immobility ▪ Loss of function – crepitus on movement	<u>Signs (joint examination)</u> ▪ Joint tenderness – joint crepitus (crackles) ▪ Bony enlargement at affected joints – limited movement ▪ Periarticular muscle atrophy (loose piece of bone in joint) ▪ Late deformity (angulation)
<u>Primary generalized OA (PGOA)</u> <u>Nadal: (NGOA)</u> - Age & sex: young or middle aged females - Joint affected: DIP usually affected and other joints may be affected - Heberden's nodes: DIP swelling (osteophytes) - Bouchard's nodes: of the PIP - These bony swellings are firstly tender and painful but later on, presented with movement limitation	<u>Secondary OA:-</u> Usually affecting the weigh bearing joint or the previously diseased, traumatized or overly used joints <u>Example of joint presentation</u> - Hip: dull or sharp pain in trochanter, groin, anterior thigh, or knee = internal rotation and abduction are lost first - Knee: knee effusion (early) - Lumbar spine: common especially L4-L5, L5-S1

Non-nodal:

- Age & sex: young or middle-aged and equal in both sexes
- Joint affected: any joint (e.g. knee, hip, hand, and spine)
- Shoulder, elbow, wrist and ankle are less common sites

- **Intervertebral** discs herniation presented with neurological deficits as Sciatica or claudication
- **Cervical** spine: common, especially in lower cervical area – neck pain may be headach

N.B.: OA of MCP joints can be seen in hemochromatosis or chondrocalcinosis

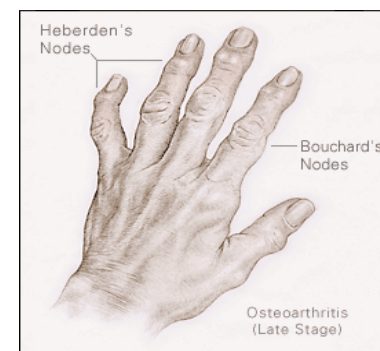
Investigation

Laboratory results are normal in OA **Normal CBC and ESR – negative RF and ANA**

X-ray: (4 classic findings)

- Narrowing of joint space – loss of cartilage
- Geode formation (intraosseous cysts)
- Sclerosing of the adjacent bone (subchondral sclerosis: "seagull sign")
- Osteophytes (bony processes)

Synovial fluid:- -Increased viscosity – low cell count - Normal glucose and protein levels



Treatment

A) Non pharmacological

- Reduction of body weigh
- **Dietary:** diet high in saturated fat may also contribute to cartilage destruction. Adequate intake of vitamin C, vitamin E, and beta-carotene may slightly reduce the risk of disease progression.
- **Physical therapy and exercise:** strengthen the muscles around affected joints (swimming is ideal for most joints)
- **Devices:** wearing a knee brace – using shoe insoles

B) Pharmacological

1- Analgesics:

- **Acetaminophen:** the first-line treatment for pain
- **NSAIDs:** NSAIDs is the second line of osteoarthritis (Monitoring of blood pressure, hematocrit, KFTs and LFTs)
- **The selective COX-2 inhibitors:** have similar efficacy to nonselective with less gastric and renal toxic
- **Steroid has No role in oseoarthrosis**

2- Glucosamine and chondroitin sulfate:

SE: - Insulin resistance - Photosensitivity - Hypertension
- proteinuria - elevated serum creatine kinase (CK)

3- Intra-articular therapy

- **Glucocorticoids:** can reduce pain and inflammation
- **Viscosupplements:** Hyaluronic acid is a glycosaminoglycan

C) Surgical treatment: joint osteotomy, total/partial joint replacement, fusion

Differential diagnosis of arthritis

	Monoarticular	Polyarticular
Collagen		Seropositive:- Rh arthritis – SLE – Scleroderma – polymyositis – dermatomyositis – Mixed connective tissue disease Vasculitis: polyarteritis nodosa (PAN) Seronegative: Ankylosing spondylitis - psoriatic – IBD arthritis
CT		Hypermobility syndrome Ehlers – Danlos – Marfan's
Infectious	Septic: Viral infections: Parvovirus B19 Enteroviruses, EBV or HIV Bacterial infections: Gonococcal, S. Aureus, Strept, Gram-negative, SBE	Post infection: reactive arthritis – rheumatic fever Other infections: Lyme disease, TB, Fungal, Leptospirosis
Crystals:	Acute Gout – pseudogout	Chronic Gout
Degenerative:	Secondary osteoarthritis - Neuropathic joints	- Primary generalized osteoarthritis (PGOA) - (NGOA)
Neoplasm:-	Primary neoplasm	- Metastases - Multiple myeloma
Miscellaneous:-	Trauma	- Sarcoidosis - Hypertrophic P. Osteoarthropathy - Osteomalacia - Drug/serum reactions
Endocrinal: Hypothyroidism – Acromegaly – Hyperparathyroidism – Hyperthyroidism		
Haematological: Haemarthrosis – Henoch-Shoenlein purpura		
Metabolic: Wilson's diseases – Haemochromatosis – Amyloidosis - Hyperlipidaemia		

Differential diagnosis of acute arthritis:

Acute traumatic: History of joint trauma (usually **knee**)

Flared osteoarthritis: History of joint symptoms and overuse

Pseudogout: ± Fever – common in knee, ankle, shoulder or wrist (**monarticular**)

Gout: Fever + First MTP, knee, ankle, and wrist. (Firstly **monarticular**)

Reiter's syndrome: Fever + Acute arthritis in young men

Gonococcemia: Fever + skin lesions + Acute arthritis (**Mono or polyarticular**)

Non-gonococcal: Fever + Monarticular of large joint

SLE: Multisystemic + knee and finger (**PIP**)

Rheumatoid A: ± Fever + **Polyarticular of small joint (stiffness)**

Eryth. Nodosum: Skin lesions + Ankles usually involved

Acute rheumatic fever: Fever + Classic migratory polyarthritis **of the big joint.**